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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/520,004	03/06/2000	John Paul Maye	046436-5016	7731
21874 7590 12/11/2008 EDWARDS ANGELL PALMER & DODGE LLP P.O. BOX 55874 BOSTON, MA 02205				
EXAMINER STULIL, VERA				
ART UNIT		PAPER NUMBER		
1794				
MAIL DATE		DELIVERY MODE		
12/11/2008		PAPER		

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

09/520,004

Applicant(s)

MAYE ET AL.

Examiner

VERA STULII

Art Unit

1794

Period for Reply -- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 19 September 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 2-21 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 2-21 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)
- 4) ☐ Interview Summary (PTO-413)
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 09/19/2008 has been entered.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 2-6, 8-11, 14-15 and 20-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Todd, Jr. et al. (US 5,082,975) for the reasons given in the previous Office action mailed March 8, 2007.

The reference and rejection are incorporated as cited in the previous Office action.

Claims 7 and 16-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Todd, Jr. et al. (US 5,082,975) in view of Simpson (Synergism Between Hop Resins and Phosphoric Acid And Its Relevance To The Acid Washing of Yeast).

The reference and rejection are incorporated as cited in the previous Office action.

Claims 12-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Todd, Jr. et al. (US 5,082,975) in view of Simpson (Synergism Between Hop Resins and Phosphoric Acid And Its Relevance To The Acid Washing of Yeast) and further in view of Todd, Jr. (US 4,002,683) hereinafter '683 Patent.

The reference and rejection are incorporated as cited in the previous Office action.

Response to Arguments

Applicant's arguments filed 09/19/2008 have been fully considered but they are not persuasive.

On page 6 paragraph 4, page 8 paragraph 2 and page 9 paragraphs 2 and 4 of the Reply to the Office action mailed March 19, 2008, Applicant states that "The Todd examples do not show treatment of any media with alkaline hop acid solutions. Todd also does not disclose treatment pre-fermentation of the yeast growing tank, fermentation tank, fermentable feed or the yeast itself, which is an aspect of the instantly claimed technology". In regard to this argument it is noted that, Todd, Jr. et al. (US Patent 5,082,975) disclose synthesis of hydrogenated purified beta acid (hexahydrolupulone) and its use as a selective inhibitor of cell growth (Col. 2 lines 33-41, Col. 3 lines 7-20). Todd, Jr. et al. disclose "[a] process for producing hexahydrolupulone which comprises of the steps of contacting beta acids in an alkaline solution with a metal oxide, hydroxide, or salt" (Col.2 lines 33-36). Todd, Jr. et al. disclose "the addition of hexahydrolupulone to a yeast culture to inhibit the growth of Lactobacillus therein" (Col. 3 lines 7-8). Todd, Jr. et al. disclose "the inhibition of a

Lactobacillus microorganism in the presence of yeast without inhibiting growth of the yeast by the application of a Lactobacillus-inhibiting amount of hexahydrolupulone thereto" (Col. 3 lines 9-11). Todd Jr. et al. disclose "the selective inhibition of one microorganism in the presence of another by the application of an amount of hexahydrolupulone which is inhibitory as to the one microorganism but not the other" (Col. 3 lines 16-19). Todd, Jr. et al. disclose that "[t]he resulting pure hexahydrolupulone is useful as a growth inhibitor in such forms as a stable alkaline solution in water" (Col. 3 lines 40-43). Todd, Jr. et al. disclose that "[s]imilar treatment of a 10% sugar solution, inoculated with yeast, did not inhibit fermentation. Accordingly, it is evident that the hexahydrolupulone solution may be used to selectively inhibit growth of specific cell lines, for example, the selective inhibition of Lactobacillus in the presence of yeast. Moreover, its use in inhibiting Lactobacillus infections in the brewhouse will become immediately apparent to one skilled in the brewing art. Other useful applications in fermentation processes, as well as pharmaceutical applications, will also be apparent to one skilled in the art" (Col. 8 lines 3-13).

In summary, Todd, Jr. et al disclose the inhibition of an unwanted cell growth (Lactobacillus) when adding a stable alkaline solution of hexahydrolupulone to a yeast culture, the fact that the treatment of a solution inoculated with yeast with a stable alkaline solution of hexahydrolupulone did not inhibit the fermentation, useful applications of such treatment techniques in brewhouses and various fermentation processes. Therefore Todd, Jr. discloses treatment of various media with alkaline hop acid solutions (Col. 8 lines 3-13). Todd Jr. discloses that addition of stable alkaline

solution of hexahydrolupulone did not inhibit the fermentation, and therefore the alkaline solution is expected to be added prior to fermentation. Todd, Jr. discloses application of such technique in brewhouses and fermentation processes. Addition of hops/hop extracts to the wort during various stages of beer production was well known in the art. Since Todd, Jr. discloses addition of stable alkaline solution of hexahydrolupulone to the fermentable solutions inoculated with yeast in order to inhibit the growth of unwanted bacteria in various fermentation processes, and since addition of hops to the wort during various stages of beer production was well known in the art, one of ordinary skill in the art would have been motivated to employ the technique as disclosed by Todd, Jr. and to add a stable alkaline solution of hexahydrolupulone to the yeast and/or to the fermentable solution inoculated with yeast as disclosed by Todd, Jr.

Applicant disagrees with the statement, that alkaline solution is expected to be added prior to fermentation (page 7 paragraph 1). Applicant's arguments are not deemed persuasive for the following reasons. Todd is concerned with viability of yeast cells and growth of yeast cells by disclosing that "the inhibition of a Lactobacillus microorganism in the presence of yeast without inhibiting growth of the yeast by the application of a Lactobacillus-inhibiting amount of hexahydrolupulone thereto" (Col. 3 lines 9-11). Therefore, one of ordinary skill in the art would have been motivated to modify Todd, Jr. and to employ Lactobacillus-inhibiting amount of hexahydrolupulone during the stage of yeast growth, i.e. prior to fermentation.

In response to Applicant's arguments regarding declaration under 37 CFR 1.132 (page 8 paragraph 3 of the Reply), it is noted that declaration states that one of ordinary

skill in this field would not have expected the use of hop acids in the manner claimed in the above-identified application to have any appreciable effects on fuel ethanol production (page 2 of declaration). This argument is not deemed persuasive for the reasons of record stated in the previous Office actions. In regard to this argument it is noted that, Todd, Jr. et al. (US Patent 5,082,975) use of hydrogenated purified beta acid (hexahydrolupulone) as a selective inhibitor of cell growth (Col. 2 lines 33-41, Col. 3 lines 7-20). Todd, Jr. et al. disclose "the addition of hexahydrolupulone to a yeast culture to inhibit the growth of Lactobacillus therein" (Col. 3 lines 7-8). Todd, Jr. et al. disclose "the inhibition of a Lactobacillus microorganism in the presence of yeast without inhibiting growth of the yeast by the application of a Lactobacillus-inhibiting amount of hexahydrolupulone thereto" (Col. 3 lines 9-11). Todd, Jr. et al. disclose that "[a]ccordingly, it is evident that the hexahydrolupulone solution may be used to selectively inhibit growth of specific cell lines, for example, the selective inhibition of Lactobacillus in the presence of yeast. Moreover, its use in inhibiting Lactobacillus infections in the brewhouse will become immediately apparent to one skilled in the brewing art. Other useful applications in fermentation processes, as well as pharmaceutical applications, will also be apparent to one skilled in the art" (Col. 8 lines 3-13). As stated above, Todd is concerned with viability of yeast cells and growth of yeast cells by disclosing that "the inhibition of a Lactobacillus microorganism in the presence of yeast without inhibiting growth of the yeast by the application of a Lactobacillus-inhibiting amount of hexahydrolupulone thereto" (Col. 3 lines 9-11). Therefore, one of ordinary skill in the art would have been motivated to modify Todd, Jr.

and to employ Lactobacillus-inhibiting amount of hexahydrolupulone during the stage of yeast growth, i.e. prior to fermentation.

On page 9 of the Reply (paragraph 2), Applicant states that "Simpson relates to a study of acid washing of pitching yeast slurries. Thus, Simpson relates to used yeast (that is, post fermentation), which is different and distinguishable from Applicants' pre-fermentation technology. As such, Simpson fails to disclose treatment pre-fermentation of the growing tank, fermentation tank, fermentable feed or the yeast itself which is an aspect of the instantly claimed technology". In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Simpson discloses that hop acids/resins are bactericidal to several lactobacilli and commercially available source of hop acids for inhibition of growth of lactic acid bacteria such as ISOHOPCO2N. Simpson is relied upon as a teaching of using isomerized hop acids in inhibiting of lactic acid bacteria. As stated in the previous Office Action, Simpson discloses that hop acids present in the brewery yeast slurries have a bacterial action on lactic acid bacteria during the acid washing process (p. 405). Simpson disclose introduction into microorganisms of aqueous solution of "isomerised hop extract (ISOHOPCO2N, Pauls Hop Products, England) hopped to a level of 60° EBCBU" (p. 406). Simpson also discloses that solution contains 0-85% NaCl (p. 406). Thus Simpson discloses alkaline aqueous solution of isomerized hop acid. Simpson also discloses that alkaline aqueous solution

of isomerized hop acid is maintained at 5° C (p. 406). As evidenced by Kaneda et al (Beer Absorption on a Lipid Membrane as Related to Sen Evaluation), the concentration of isomerized acids in ISOHOPCO2N product is 30%, in particular the concentration of isohumulone (isoalpha acid) is 21.6%.

In summary, Simpson discloses that hop acids/resins are bactericidal to several lactobacilli and the fact that ISOHOPCO2N is used as a commercially available source of hop acids for inhibition of growth of lactic acid bacteria. Since Todd Jr. et al disclose aqueous hop acid alkaline solution as a selective inhibitor of cell growth, and Simpson discloses that hop acids have a bacterial action on lactic acid bacteria and adding aqueous isoalpha acid alkaline solution to yeast, it would have been obvious to modify disclosure of Todd et al and substitute synthesized hexahydrolupulone with commercially available aqueous isoalpha hop acid alkaline solution (ISOHOPCO2N) as a cell growth inhibitor in order to simplify the process and avoid multiple steps of hexahydrolupulone synthesis.

In response to Applicant's arguments regarding rejection of claims 12 and 13 (pages 9 and 10 of the reply), Applicant is referred to the response to arguments above.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to VERA STULII whose telephone number is (571)272-3221. The examiner can normally be reached on 7:00 am-3:30 pm, Monday-Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Keith Hendricks can be reached on (571) 272-1401. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Steve Weinstein/
Primary Examiner, Art Unit 1794

VS